

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/SA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2004/009043

International filing date (day/month/year)
12.08.2004

Priority date (day/month/year)
12.08.2003

International Patent Classification (IPC) or both national classification and IPC
C07K14/81, A61L2/00

Applicant
OCTAPHARMA AG

1. This opinion contains indications relating to the following items:

- | | |
|---|---|
| <input checked="" type="checkbox"/> Box No. I | Basis of the opinion |
| <input type="checkbox"/> Box No. II | Priority |
| <input type="checkbox"/> Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> Box No. V | Reasoned statement under Rule 43bis.1 (a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> Box No. VI | Certain documents cited |
| <input type="checkbox"/> Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> Box No. VIII | Certain observations on the international application |

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/SA220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/SA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

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Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-11
	No: Claims	12-19
Inventive step (IS)	Yes: Claims	
	No: Claims	1-19
Industrial applicability (IA)	Yes: Claims	1-19
	No: Claims	

2. Citations and explanations

see separate sheet

1. The application discloses a process for preparing A1AT from solution comprising the steps of a) ion exchange chromatography, b) virus inactivation by detergent and optionally additional virus inactivating substances, and c) salting out of the detergent. The effect is not only removal of the detergent but also removal of contaminating proteins.

2. Novelty (Art. 33(2) PCT)

Product claims 12 to 19 lack novelty in view of the A1AT preparations disclosed in EP436086, DE4407837 and WO98/56821. All three documents disclose A1AT of high purity. Example 2 of WO98/56821 uses an AAT produced by SERVA which according to the manufacturers specification is already 95% pure and has an activity of 0.81 PEU. According to Table 2, the product obtained by the method of Expl. 2 is >100% pure and has a specific activity of 1 PEU. Experimental evidence about the IgA content of the preparations obtained according to the three cited documents is not available. Therefore, also the products of EP436086 and DE4407837 are considered to be falling within the terms of the claims. Claims 13 to 17 lack novelty because they are directed to products obtainable by the claimed method, i.e. they are directed to the products per se.

3. Inventive step (Art. 33(3) EPC)

Claims 1 to 19 are considered to lack an inventive step in view of WO94/26287 (D1). D1 discloses a process for reduction of virus inactivating chemicals and/or detergents in an aqueous solution containing a plasma protein. The process comprises the salting out of e.g. TnBP/Triton X-100 by increasing e.g. the sodium citrate concentration (cf. examples). This document discloses all the characteristic features of the presently claimed method. It only differs by not mentioning A1AT as a plasma protein. But D1 generically refers to plasma proteins. Therefore, if the person of skill was looking for a way of reducing antiviral chemicals/detergents in a solution comprising A1AT (which is a plasma protein), D1 provided an obvious solution. The features of claims 6 to 10 for the further purification are also known to the person of skill and represent obvious further process steps.

The applicant mentions in the description (pp. 4/5) that the person of skill would have hesitated to apply the procedure of D1 in view of Expl. 4 showing the residual concentrations of Triton X-100 and TnBP to be above pharmacologically acceptable levels. However, D1 specifically discusses these residual levels and

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explains them as a peculiarity in the case of albumin because this protein binds hydrophobic agents. In Expls. 1 to 3, the residual levels of detergent and TnBP are way below the pharmacologically acceptable threshold. The person of skill would therefore have a reasonable expectation of success.